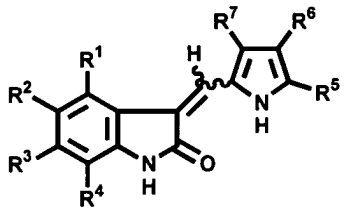
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (original) A solid formulation, said formulation comprising 5 – 60 % w/w of an indolinone of formula I:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_rR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$,
$-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^6 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of -$(CH_2)_4$-, -$(CH_2)_5$- and -$(CH_2)_6$-;

with the proviso that at least one of R^5, R^6 or R^7 must be

-$C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is -$N(R^{11})(CH_2)_nR^{12}$ or -$NHCH_2CH(OH)CH_2R_{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of –$NR^{13}R^{14}$, –$N^+(O^-)R^{13}R^{14}$, –$N(OH)R^{13}$, and –$NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, -$C(O)R^{15}$, -$NR^{13}R^{14}$ and -$C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; or

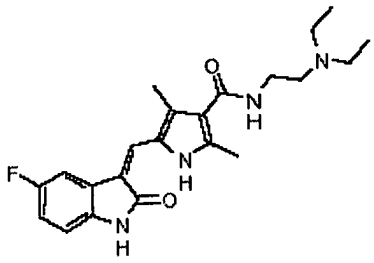
pharmaceutically active salts of the compound of formula I; and

a pharmaceutically acceptable carrier therefor comprising 10 – 86 % w/w of one or more pharmaceutically acceptable diluents, 2 – 20 % w/w of one or more pharmaceutically acceptable binders, 2 – 20 % w/w of one or more pharmaceutically acceptable disintegrants, and 1 – 10 % w/w of one or more pharmaceutically acceptable lubricants.

2. (original) The formulation of claim 1, wherein the salt of said indolinone is the malate salt.

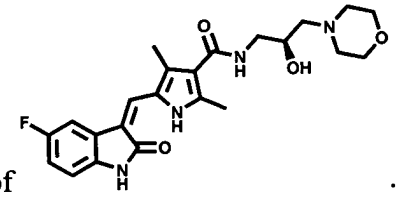
3. (original) The formulation of claim 1, wherein the salt of said indolinone is the maleate salt.

4. (original) The formulation of claim 1, wherein the salt of said indolinone is the



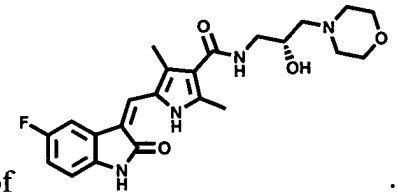
L-malate salt of

5. (original) The formulation of claim 1, wherein the salt of said indolinone is the



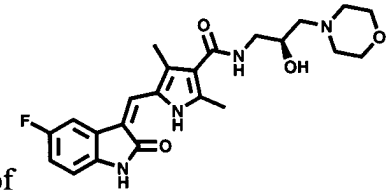
maleate salt of

6. (original) The formulation of claim 1, wherein the salt of said indolinone is the

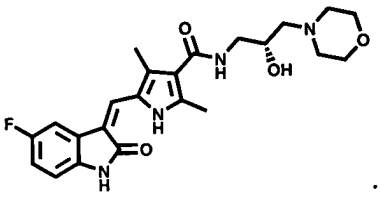


maleate salt of

7. (original) The formulation of claim 1, wherein the salt of said indolinone is a



mixture of the maleate salt of and



8. (original) The formulation of claim 1, wherein each of said one or more pharmaceutically acceptable diluents is selected from the group consisting of pregelatinized

starch, lactose monohydrate, lactose monohydrate regular grade, mannitol, calcium phosphate and microcrystalline cellulose.

9. (original) The formulation of claim 1, wherein each of said one or more pharmaceutically acceptable binders is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethyl cellulose, hydroxypropylcellulose and starch.

10. (original) The formulation of claim 1, wherein each of said one or more pharmaceutically acceptable disintegrants is selected from the group consisting of crosscarmellose sodium, sodium starch glycolate, crospovidone, and starch.

11. (original) The formulation of claim 1, wherein each of said one or more pharmaceutically acceptable lubricants is selected from the group consisting of magnesium stearate, sodium stearyl fumarate, glyceryl behenate and stearic acid.

12. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 5 – 55 % w/w.

13. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 10 – 60 % w/w.

14. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 15 – 50 % w/w.

15. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 35– 45 % w/w.

16. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 39 – 43 % w/w.

17. (canceled)

18. The (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 10 – 40 % w/w.

19. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 20 – 50 % w/w.

20. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 38 – 42 % w/w.

21. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 38 – 41 % w/w.

22. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 39 – 41 % w/w.

23. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 10 – 45 % w/w.

24. (currently amended) The formulation of claim 1, wherein the amount of indolinone or pharmaceutically acceptable salt thereof is from 15 – 40 % w/w.

25. (original) The formulation of claim 1, wherein the amount of diluent is from 10 – 80 % w/w.

26. (original) The formulation of claim 1, wherein the amount of diluent is from 20 – 86% w/w.

27. (original) The formulation of claim 1, wherein the amount of diluent is from 30-80 % w/w

28. (original) The formulation of claim 1, wherein the amount of diluent is from 10 – 25 % w/w.

29. (original) The formulation of claim 1, wherein the amount of diluent is from 25 – 50 % w/w.

30. (original) The formulation of claim 1, wherein the amount of diluent is from 34 – 60 % w/w.

31. (original) The formulation of claim 1, wherein the amount of diluent is from 34 – 77%.

32. (original) The formulation of claim 1, wherein the amount of diluent is from 45-65 % w/w.

33. (original) The formulation of claim 1, wherein the amount of diluent is from 39 – 80 % w/w

34. (original) The formulation of claim 1, wherein the amount of diluent is from 45 – 49 % w/w.

35. (original) The formulation of claim 1, wherein the amount of diluent is from 46 – 50 % w/w.

36. (original) The formulation of claim 1, wherein the amount of diluent is from 45 – 48 % w/w.

37. (original) The formulation of claim 1, wherein the amount of diluent is from 46 – 48 % w/w.

38. (original) The formulation of claim 1, wherein the amount of binder is from 2 – 10 % w/w.

39. (original) The formulation of claim 1, wherein the amount of binder is from 5 – 20 % w/w.

40. (original) The formulation of claim 1, wherein the amount of binder is from 5 – 10 % w/w.

41. (original) The formulation of claim 1, wherein the amount of binder is from 3 – 6 % w/w.

42. (original) The formulation of claim 1, wherein the amount of binder is from 3 – 8 % w/w.

43. (original) The formulation of claim 1, wherein the amount of binder is from 4 – 6 % w/w.

44. (canceled)

45. (original) The formulation of claim 1, wherein the amount of binder is from 4 – 8 % w/w.

46. (original) The formulation of claim 1, wherein the amount of binder is from 5 – 9 % w/w.

47. (original) The formulation of claim 1, wherein the amount of binder is from 4 – 7 % w/w.

48. (original) The formulation of claim 1, wherein the amount of binder is from 5 – 7 % w/w.

49. (original) The formulation of claim 1, wherein the amount of disintegrant is from 2 – 10 % w/w.

50. (original) The formulation of claim 1, wherein the amount of disintegrant is from 5 – 20 w/w.

51. (original) The formulation of claim 1, wherein the amount of disintegrant is from 5 – 10 % w/w.

52. (original) The formulation of claim 1, wherein the amount of disintegrant is from 4 – 8 % w/w.

53. (original) The formulation of claim 1, wherein the amount of disintegrant is from 5 – 8 % w/w.

54. (original) The formulation of claim 1, wherein the amount of disintegrant is from 3 – 7 % w/w.

55. (original) The formulation of claim 1, wherein the amount of disintegrant is from 3 – 6 % w/w.

56. (original) The formulation of claim 1, wherein the amount of disintegrant is from 4 – 6 % w/w.

57. (canceled)

58. (canceled)

59. (original) The formulation of claim 1, wherein the amount of lubricant is from 1 – 5 % w/w.

60. (canceled)

61. (original) The formulation of claim 1, wherein the amount of lubricant is from 1 – 2 % w/w.

62. (original) The formulation of claim 1, wherein the amount of lubricant is from 1 – 1.5 % w/w.

63. (original) The formulation of claim 1, wherein the amount of lubricant is from 1 – 2.5 % w/w.

64. (original) The formulation of claim 1, wherein the amount of lubricant is from 1.3 – 1.7 % w/w.

65. (original) The formulation of claim 1, wherein the amount of lubricant is from 1.4 – 1.8 % w/w.

66. (original) The formulation of claim 1, wherein the amount of lubricant is from 1.3 – 1.6 % w/w.

67. (original) The formulation of claim 1, wherein the amount of lubricant is from 1.4 – 1.6 % w/w.

68. (original) The formulation of claim 1, wherein said diluent is mannitol.

69. (original) The formulation of claim 1, wherein said binder is polyvinylpyrrolidone.

70. (original) The formulation of claim 1, wherein said disintegrant is crosscaramellose sodium.

71. (original) The formulation of claim 1, wherein said lubricant is magnesium stearate.

72. (original) The formulation of claim 1, wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_rR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen and alkyl;

R^6 is $-C(O)R^{10}$ wherein R^{10} is $-NR^{11}(CH_2)_nR^{12}$ wherein:

R^{11} is hydrogen or lower unsubstituted alkyl;

n is 2 or 3; and

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O^-)R^{13}R^{14}$, and $-N(OH)R^{13}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl and heteroaryl;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, lower alkyl substituted with hydroxy, alkylamino, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$; and

r is 1, 2, 3, or 4.

73. (original) The formulation of claim 1, wherein R^6 is $-C(O)R^{10}$ wherein R^{10} is $-NHCH_2CH(OH)CH_2R_{12}$, wherein R_{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O^-)R^{13}R^{14}$ and $-N(OH)R^{13}$; and R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, lower alkyl substituted with hydroxy, alkylamino, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group.

74. (original) The formulation of claim 1, wherein R^6 is $-C(O)R^{10}$ wherein R^{10} is $-NR^{11}(CH_2)_nR^{12}$ wherein:

R^{11} is hydrogen or lower unsubstituted alkyl;

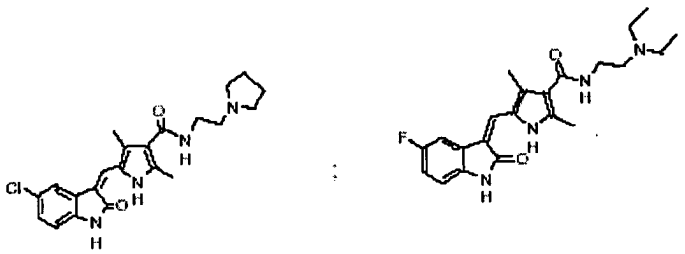
n is 2 or 3; and

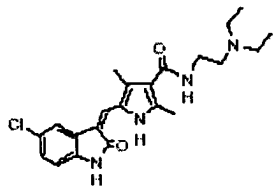
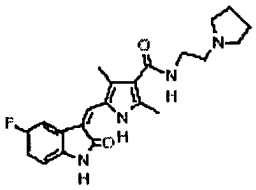
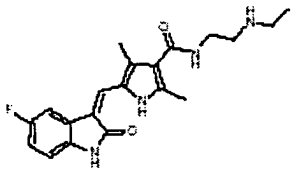
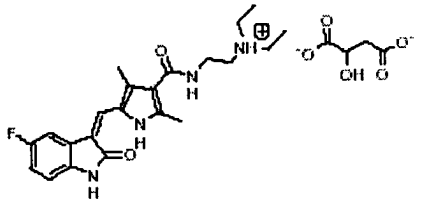
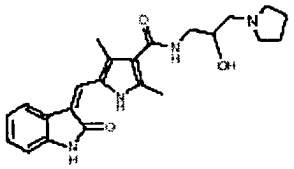
R^{12} is $-NR^{13}R^{14}$ wherein R^{13} and R^{14} are independently unsubstituted lower alkyl; and

R^7 is selected from the group consisting of hydrogen, alkyl, aryl and heteroaryl.

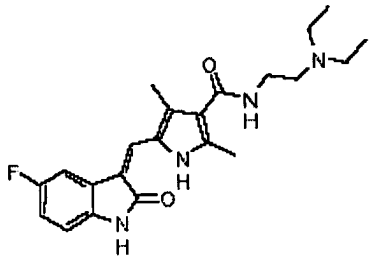
75. (original) The formulation of claim 1, wherein R^6 is N-(2-dimethylaminoethyl)aminocarbonyl, N-(2-diethylaminoethyl)-N-methylaminocarbonyl, N-(3-dimethylaminopropyl)aminocarbonyl, N-(2-diethylaminoethyl)aminocarbonyl, N-(2-ethylaminoethyl)aminocarbonyl, N-(3-ethylaminopropyl)aminocarbonyl, N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-aminocarbonyl, N-(2-pyrrolidin-1-yl-ethyl)-aminocarbonyl or N-(3-diethylaminopropyl)aminocarbonyl.

76. (currently amended) The formulation of claim 1, wherein the compound of formula I is selected from the group consisting of:







; and


77. (original) The formulation of claim 1, wherein the compound of formula I is:



78. (canceled)

79. (original) The formulation of claim 1, wherein said formulation comprises 30 – 50 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 35 – 60 % w/w mannitol, 5 – 8 % w/w croscaramellose sodium, 4 – 6 % w/w povidone and 1 – 2 % w/w magnesium stearate.

80. (original) The formulation of claim 1, wherein said formulation comprises 40 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 47.5 % w/w mannitol, 6 % w/w croscaramellose sodium, 5 % w/w povidone and 1.5 % w/w magnesium stearate.

81. (original) The formulation of claim 1, wherein said formulation comprises 10 – 16 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 65 – 80 % w/w mannitol, 5 – 10 % w/w croscaramellose sodium, 4 – 8 % w/w povidone and 1 – 2 % w/w magnesium stearate.

82. (original) The formulation of claim 1, wherein said formulation comprises 15.2 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 72.7 % w/w mannitol, 6 % w/w croscaramellose sodium, 5.1 % w/w povidone and 1 % w/w magnesium stearate.

83. (original) The formulation of claim 1, wherein said formulation comprises 38 – 42 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 45 – 49 % w/w mannitol, 4 – 8 % w/w croscaramellose sodium, 3 – 7 % w/w povidone and 1.3 – 1.7 % w/w magnesium stearate.

84. (original) The formulation of claim 1, wherein said formulation comprises 39 – 43 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 46 – 50 % w/w mannitol, 5 – 9 % w/w croscaramellose sodium, 4 – 8 % w/w povidone and 1.4 – 1.8 % w/w magnesium stearate.

85. (original) The formulation of claim 1, wherein said formulation comprises 38 – 41 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 45 –

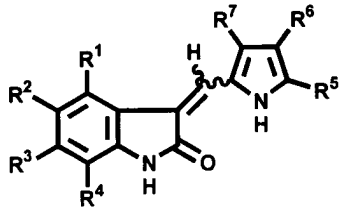
48 % w/w mannitol, 4 – 7 % w/w croscaramellose sodium, 3 – 6 % w/w povidone and 1.3 – 1.6 % w/w magnesium stearate.

86. (canceled)

87. (original) The formulation of claim 1, wherein said formulation comprises 39 – 41 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 46 – 48 % w/w mannitol, 5 – 7 % w/w croscaramellose sodium, 4 – 6 % w/w povidone and 1.4 – 1.6 % w/w magnesium stearate.

88-91. (canceled)

92. (original) A solid formulation, said formulation comprising 5 – 60 % w/w of the malate salt of an indolinone of formula I:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_rR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$,
$-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^6 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$;

with the proviso that at least one of R^5, R^6 or R^7 must be $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R_{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O^-)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; and

a pharmaceutically acceptable carrier therefor comprising 10 – 86 % w/w of one or more pharmaceutically acceptable diluents, 2 – 20 % w/w of one or more pharmaceutically acceptable binders, 2 – 20 % w/w of one or more pharmaceutically acceptable disintegrants, and 1 – 10 % w/w of one or more pharmaceutically acceptable lubricants.

93 - 106. (canceled)